A Trusted Name For Over Half A Century

PUREPAC

Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
908-527-9100
Fax: 908-355-7048

RICHARD F. MOLDIN
President and Chief Executive Officer

November 2, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Comments on Proposed Rule Regarding 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications

Dear Sir or Madam:

Purepac Pharmaceutical Co. has reviewed the proposed rule regarding the 180-day generic drug exclusivity and respectfully submits the following comments for the agency's consideration.

The statutory provision for generic drug exclusivity was intended to provide an incentive for sponsors to challenge innovators' patents and accelerate market entry of competitively-priced generic drug products. Thus the economic benefit of an exclusive marketing position secured by a single applicant was intended to be balanced with a significant benefit to the U.S. consumer. Since the enactment of Waxman-Hatch, and most notably following the *Mova* and *Granutec* decisions, the generic drug exclusivity provision has degraded into a vehicle that is commonly used to capture significant monetary benefits for a single sponsor while depriving the U.S. consumer of the benefit of lower cost medication.

While selected sponsors have enjoyed economic windfalls, subsequent applicants otherwise eligible for ANDA approval remain in limbo. Additionally, the integrity of the ANDA submission process has been seriously compromised by sponsors who resort to the submission of substantially flawed or "sham" applications in order to secure the exclusivity seat assigned to the first ANDA containing a Paragraph IV certification that is accepted for filing. Since ANDA filing acceptance does not involve a substantive review of the submission, sponsors are able to secure first-to-file status with ANDA's that are substantially

85N-0214 C56

flawed and require extraordinary amendment. This abusive practice has delayed market formation for several important generic products and should be viewed with the same level of concern as a financial arrangement between innovator and ANDA sponsor.

In the absence of a statutory remedy for the situation that the industry is facing, the agency must promulgate regulations that will minimize the potential for abuse. These regulations cannot and should not be inconsistent with the express language of the statute. They must follow its provisions while building in administrative remedies that are clearly within the agency's discretion and area of oversight. These concepts form the basis for our Company's position on the elements of the proposed rule, as outlined below.

Only First Applicant Eligible

Purepac disagrees with this proposal insofar as it provides that where an applicant initially gains first-to-file status but is subsequently found ineligible "[n]o other applicant with a paragraph IV certification will be eligible for exclusivity." We believe that exclusivity should pass to the next applicant in line in the event that the first applicant becomes ineligible at any point during the pendency of its application. Awarding eligibility to a subsequent applicant would not violate the language of the statute. It would ensure that an applicant who is truly qualified—*i.e.*, the first to submit an ANDA that is both substantially complete and contains a paragraph IV certification to a listed patent—is not unfairly disadvantaged by a lack of diligence on the part of the prior applicant.

The agency must recognize that its present proposal is likely to introduce yet another pathway for abuse of the exclusivity provision. For example, an applicant who is struggling or lagging behind in its efforts to develop a non-infringing product may decide to take a "submit as is" approach and file an incomplete or sham application, knowing that it will suffer no ill effect as a result. This may be viewed as a "win-win" approach by a less scrupulous applicant given the two possible outcomes: (1) the applicant could gain and retain exclusivity in the event that it was first to file and the agency did not recognize and rectify the improper conduct; or (2) if the applicant is later stripped of eligibility, it would have succeeded in eliminating exclusivity for the product altogether, and thereby removed a marketing barrier that would have

otherwise kept the applicant off the market during a competitors' rightfully-earned period of exclusivity.

Only by providing for exclusivity to pass to the next eligible applicant can the agency prevent the use of such spoiler tactics. In evaluating the comments that preceded the 1994 Final Rule, the agency dismissed the concern expressed by industry regarding "sham" applications. With the removal of the "successful defense" requirement, the agency must recognize that this form of abuse has become a reality that has compromised the good faith efforts and investments of diligent ANDA sponsors. Purepac urges the agency to implement regulations that establish significant disincentives for firms that engage in this and any other form of inequitable conduct.

Grounds for Disqualification

Unacceptable bioequivalence study

Purepac fully supports the provision that would require FDA to revoke eligibility in the event that the bioequivalence study, upon full review, does not meet agency standards for approval. However, we believe that this provision should be reserved for those situations in which a failing study, or a study whose design is contrary to well-established scientific and/or regulatory principles is submitted in the original application. The provision should not be applied to those situations that are outside of the control of the applicant. For example, if an in-vivo/in-vitro guidance were to change while an application was pending, and the applicant was asked to conduct additional work, the applicant's eligibility should not be revoked.

Substantially flawed submission

Purepac urges the agency to adopt a regulation that would enable disqualification in the event that an application is found to be substantially flawed following full review. The present proposal provides a disincentive for submission of an inadequate bioequivalence study. Purepac fully supports this provision. However, we believe that there are other situations that should warrant disqualification, and that the agency should develop the regulation accordingly. For example, if upon full review of the application, the formulation was determined to be

inherently unstable, the applicant would have to engage in a reformulation exercise and substantially modify the CMC section of its application when the work was completed. It would be extremely inequitable if the agency were to reserve the exclusivity seat for the "first" applicant under these circumstances.

As stated in our previous comments, Purepac believes that exclusivity should pass to the next applicant in line in the event that the first applicant becomes ineligible. We realize that this may pose administrative difficulties for the agency in terms of tracking the first filed position. To simplify matters, we suggest that the agency promptly return substantially flawed applications to their sponsors with a letter stating that a new ANDA may be filed when the situation is corrected. The agency should retire the original ANDA number and assign a new one if the applicant files a new submission at a future date. This would provide a relatively straight-forward means of determining which applicant occupies the exclusivity seat at any given point in time.

New paragraph IV certification

The proposed rule contains a provision that would enable FDA to revoke eligibility in the event that the applicant submits a new paragraph IV certification. Reformulation is given as an example of a situation that would result in a new certification. Purepac supports the intent of this provision, because a significant change to the application could result in a product that is substantially different than the one that was purported when the applicant secured the exclusivity seat. This represents a tremendous inequity because subsequent applicants who exercised diligence in developing and filing an ANDA for a quality, non-infringing product will be delayed by the activities associated with the first applicant's reformulation (e.g. stability testing, new bioequivalence study, ANDA amendment or supplement, etc.). Furthermore, the basis for the first applicant's claim of non-infringement may have changed as a result of the change in the conditions of the application.

In order to ensure that the proposed provision is effectively and equitably applied, Purepac urges that the agency define, via regulation, those situations that require a new paragraph IV certification following the original submission.

Purepac also believes, however, that there should be an exception to this rule which would allow an applicant to amend its paragraph IV certification, without resulting in a loss of eligibility, to reflect its acquisition of a license to a listed patent. Negotiation of a patent license is often the most economical and time-effective manner of compromising a dispute regarding infringement or validity of a given patent. It should not necessarily result in the first applicant's loss of eligibility.

First Applicant to Submit a Paragraph IV Certification on any Listed Patent Qualifies

Purepac supports this provision. However, we wish to express one specific concern that the agency should address by way of the final rule. This concern relates to the filing of a certification for a use patent claiming a use for which the applicant is not seeking approval. The 1994 rule specifically stated that an applicant does not have the option of filing a paragraph IV certification in this situation. The applicant must file a statement of non-applicability under 505(j)(2)(A)(viii).

It has become apparent (through information contained in public court documents) that some applicants are filing paragraph IV certifications for patents that solely claim a method of use for which the applicant is not seeking approval. We are unaware of any action that the agency has taken to rectify these situations. If proper oversight is not exercised, an applicant who files an improper certification of this nature may secure an unwarranted exclusivity award, or (in the event that the applicant was not first to file) may prematurely trigger the exclusivity of the first applicant.

Untimely Filed Patents

Purepac supports the agency's proposal regarding untimely filed patents, certification requirements, and granting of exclusivity under these circumstances.

Shared Exclusivity for Multiple ANDA's Filed on the Same Day

Purepac supports the agency's proposal regarding shared exclusivity for multiple applications filed on the same day. We agree that

there is no viable alternative. Furthermore, we note that although several applicants may share the exclusivity seat, the most diligent applicant (*i.e.*, the one with an ANDA approval and no remaining litigation issues) will reap the actual benefit when the trigger occurs. This further justifies the proposal.

Waiver of 180-Day Exclusivity and Relinquishing Eligibility

Purepac disagrees with the distinction drawn by the Agency between selective and non-selective waivers. We believe that an applicant should be able to assign its eligibility selectively to any other applicant at any point after a substantive review of the application has been conducted by the agency, but prior to the triggering of that applicant's 180-day period of exclusivity. For example, in the event that the first applicant is sued by a patent holder and a number of subsequent applicants are not, it would be beneficial to the public, and both applicants, if the first applicant were able to waive its exclusivity selectively in favor of one of the later applicants. The public would benefit through the introduction of a new generic product long in advance of the final resolution of the first applicant's litigation. The applicants would benefit economically through the joint exploitation of the first applicant's first-to-file status and the later applicant's freedom from patent litigation. This proposal would further promote the prompt entry of generics into commerce in situations where the first applicant did not submit a sham ANDA, but is unable to exercise its eligibility for other reasons.

Triggering Period

Purepac does not believe that the Agency's proposal with respect to the adoption of a Triggering Period is supported by, or consistent with, the express language of the Statute.

Decision of a Court

Purepac believes that this section of the proposed rule requires further clarification. The proposal explains that the (statutory) language pertaining to the first exclusivity trigger refers to a particular applicant, and that the language of the second trigger does not attach importance to the specific applicant. The statutory language has been used as the

basis to support the agency's position that the second trigger can come from a decision of any court hearing a patent infringement or declaratory judgement case involving "the patent at issue". Purepac believes that this last term requires definition in order to ensure proper and consistent commencement of exclusivity awards. While we agree with the agency's position that the statutory language for the second trigger does not attach importance to the specific applicant, we believe that it attaches importance to a specific patent, *i.e.*, the patent to which the first applicant certified paragraph IV. Therefore, we encourage the agency to clarify that a court decision in favor of a subsequent applicant must pertain to a patent to which the first applicant filed a paragraph IV certification in order to qualify as a trigger.

This concludes Purepac's response to the proposed rule regarding 180-day exclusivity for generic drug products. We trust that the agency will give appropriate consideration to all comments submitted by interested parties, and promulgate regulations commensurate with the intent of the Waxman-Hatch legislation.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

Richard F. Moldin
President and CEO

TER

Call 1-800-PICK-UPS (1-800-742-5877) or visit our Web site at www.ups.c

ace

ıg Label and your address label

acking Label to the left of the address label.

UPS Shipper Number or place parcel register tape above the address label.

pping Document

1

OM: **1 OF 1**

GULATORY AFFAIRS DEPARTMENT
EPAC PHARMACEUTICAL CO.
3) 659-2431
ELMORA AVENUE
ZABETH NJ 07207

IIP TO:

DOCKETS MANAGEMENT BRANCH (HFA-305)
FOOD AND DRUG ADMINISTRATION
5630 FISHERS LANE, ROOM 1061
OCKVILLE MD 20852

MD 2070-10

UPS NEXT DAY AIR

TRACKING #: 1Z 062 077 01 4769 7835

1